Section: General Medicine

Original Research Article

A CROSS SECTIONAL STUDY TO ESTIMATE THE INCIDENCE OF COGNITIVE IMPAIRMENT AMONG ADULTS WITH TYPE II DIABETES MELLITUS IN TERTIARY CARE CENTRE IN CHENNAI

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Abstract

Background: Diabetes mellitus (DM) is a metabolic condition marked by an increase in plasma glucose levels caused by insulin insufficiency and/or resistance. T2DM is characterized by insulin resistance, in which the body fails to create an appropriate physiological response to circulating insulin. According to a recent study by the International Diabetes Federation, 382 million people worldwide have diabetes, with the number expected to rise to 592 million by 2035. Type 2 diabetes mellitus accounts for 85 percent to 95 percent of all diabetes cases. It has risen in most countries as a result of sudden social and cultural changes, increased urbanization, changes in eating patterns, population aging, physical inactivity, and harmful behaviour. A study had shown that in type 2 diabetes, having a higher HbA1c level was linked to a deterioration in cognition among subjects with diabetes mellitus. When compared to those without DM, a recent community-based longitudinal study found that the relative risk of Alzheimer's disease (AD) and vascular dementia in the DM population was 1.46 and 2.5 respectively. Furthermore, DM has been proposed as a standalone risk factor for dementia, independent of other known risk factors such as hypertension and atherosclerosis. Effective cognitive function is required for basic survival and meaningful living, as well as to become and maintain a competent and self-sufficient person. So, early diagnosis of cognitive impairment and good glycemic control are very important to improve the quality of life in DM patients. The objective is to estimate the prevalence of cognitive impairment in patients with T2DM. **Materials and Methods:** A total of 170 diabetic patients were enrolled for the study in the age group of 30 to 50 years. The data was collected using MMSE and MOCA scale for cognitive impairment, blood glucose and urine albumin lab investigation and questionnaire for general information. The data collected were analyzed using SPSS-22 software system. The general information of DM patient and DM disorder related factors were recorded using questionnaire and with use of their diabetic records. **Result:** As per MMSE score, the mean score in our study participants was 26.7 with S.D 2.07. The score below 24 were considered to have cognitive impairment. Around 17 participants of around 10% had cognitive impairment. Score 18-23 were considered to have mild cognitive impairment. Those less than 17 were considered to have severe cognitive impairment. In our study none of the participants had severe cognitive impairment as per MMSE scale. As per MOCA score, the mean score in our study participants was 27.5 with S.D 1.86. The score below 26 were considered to have cognitive impairment. Around 17 participants of around 10% had cognitive impairment. The participants who were diagnosed to have cognitive impairment as per MOCA score were also diagnosed to have cognitive impairment as per MMSE score. Only 4.1% were belonging to age less than 35 years. Majority of the participants around 82.4% were above age 41years. The gender distribution shows 103 males and 67 females. There was higher prevalence of cognitive impairment in ages above 41 years but the results were not statistically significant. There was no significant association of gender with cognitive impairment. Patients with uncontrolled glucose level have significantly higher prevalence of cognitive impairment compared to

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controlled glucose level patients and p value is less than 0.001. There was no significant association of cognitive impairment with duration of DM in our study but there was significantly higher prevalence of cognitive impairment among patients with one or more hypoglycemic episodes compared to no hypoglycemic episodes. Hypoglycemia may raise the risk of future cognitive impairment through a variety of ways. Proteinuria and treatment modalities had no significant association with cognitive impairment. **Conclusion:** The prevalence of 10% of cognitive impairment in our study results suggest a need of routine cognitive function screening in individuals with Type 2 DM for early detection. hence, prompt psychosocial interventions can be adopted to prevent further cognitive function deterioration. We also suggest performing a prospective trial with a bigger sample size, HbA1c readings, and baseline cognitive impairment measurements to examine the effect of diabetes duration and blood sugar variation on cognitive function over time.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic condition marked by an increase in plasma glucose levels caused by insulin insufficiency and/or resistance, which can result in organ damage. Type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) are some of the major types of diabetes (T2DM). T1DM is caused by an autoimmune reaction that destroys the pancreatic beta cells, resulting in total insulin insufficiency, whereas T2DM is characterized by insulin resistance, in which the body fails to create an appropriate physiological response to circulating insulin.[1]

According to a recent study by the International Diabetes Federation, 382 million people worldwide have diabetes, with the number expected to rise to 592 million by 2035. The majority of the 382 million people are between the ages of 40 and 59. India is the second-largest diabetic country, with 65.1 million diabetics in 2013, and this number is anticipated to rise to 109 million by 2035.[2]

Type 2 diabetes is the most common type of diabetes, characterized by insulin resistance and relative insulin deficiency, and accounts for 85 percent to 95 percent of all diabetes cases. It has risen in most countries as a result of sudden social and cultural changes, increased urbanization, changes in eating patterns, population aging, physical inactivity, and harmful behavior.[2]

The effects of diabetes mellitus on the renal, cardiac, retinal, and peripheral nervous systems are well-known and widely accepted. Consistently elevated blood glucose levels are a major contributor to diabetic complications, particularly neurological symptoms. The consequences of diabetes and its impact on visual loss, neuropathy, and cardiovascular disease have gotten a lot of attention, but DM-induced cognitive dysfunction has gotten less attention and is not well known. More lately, the issue of cognitive impairment in type 2 diabetes has sparked a lot of debate.[3]

Cognitive functions denote "Acquisition, processing, integration, storage, and recovery of information". Attention, perceptions, memory, and executive function (higher-level planning and decision-making) are all part of it.[4] Because life expectancy has increased dramatically as a result of medical improvements, it has been hypothesized that the incidence of T2DM and dementia will rise as the population ages.[5] Indeed, when compared to people with normal blood glucose levels, people with T2DM have a significantly higher risk of developing cognitive impairments and dementia.[6]

Cukierman-Yaffe T et al. studied the relationship between cognitive status and hyperglycemia in 3000 people (ACCORD-MIND) and discovered that in type 2 diabetes, having a higher HbA1c level was linked to a deterioration in cognition among subjects with diabetes mellitus.[7] When compared to those without DM, a recent community-based longitudinal study found that the relative risk of Alzheimer's disease (AD) and vascular dementia in the DM population was 1.46 and 2.5 respectively. Furthermore, DM has been proposed as a standalone risk factor for dementia, independent of other known risk factors such as hypertension and atherosclerosis.[8]

Although the specific pathophysiology of DM-mediated dementia is unknown, existing evidence suggests that both cerebrovascular and neurodegenerative alterations are involved in the development and progression of DM-mediated cognitive impairment. There are currently no DM-specific medications available to prevent or improve cognitive impairment.[1] Nonetheless, antidiabetic treatments have been shown to have therapeutic potential in the treatment and prevention of cognitive impairment in several studies. The ACCORD-MIND study, the largest randomized controlled trial to date, found that the intensive glycemic control group had a considerably lower loss in total brain volume than the standard glycemic control group. The efficacy of glycemic management in protecting cerebral structure cannot be ignored, even though the cognitive outcomes were not different. These trials' findings clearly show that DM-targeted therapy could be a novel method for preventing dementia and possibly slowing its progression.[9] So, in this context, this study was conducted among DM patients on cognitive impairment.

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Objectives of the Study

Primary Objective

- To estimate the prevalence of cognitive impairment in patients with T2DM

Secondary Objective

- To determine presence of correlation between cognitive impairment and its severity with the duration of disease
- To determine presence of correlation between patients with cognitive impairment and frequency of hypoglycaemic episodes
- To determine the presence of correlation between proteinuria and cognitive impairment
- To determine the presence of correlation between cognitive impairment and grade of blood sugar control

MATERIALS AND METHODS

Study Design: Cross-sectional study

Study Duration: Feb 2020 to December 2021

Study Setting: Department of Internal medicine & Institute of Diabetology, Govt Stanley Medical College Hospital, Chennai

Target Population: Type 2 Diabetes mellitus patients

Sample Population: Type 2 Diabetes mellitus adult patients attending OPD in Govt. Stanley medical college Hospital

Inclusion Criteria

- Patients above age 30 years and below 50 years

Exclusion Criteria

- Patients with type-1 diabetes, stroke, alcohol intake or smoking habits, total blindness in both eyes, or complete loss of hearing in both ears; and patients who were previously diagnosed with and were known case of mental retardation, psychiatric disorders, any psychoactive drug use, any other known cns impairment from other medical or surgical causes, pregnant and lactating women.
- Age >50 & <30 years

Sample Size

Based on the reference study done done by Kodl et al, Minnesotta

Formula: n = Z2pq / d2

Where Z = 1.96 (statistical significant constant for 95% CI)

p =11.3% (Incidence of Cognitive impairment among young adults with Type 2 diabetes from previous study)

q = 88.7% (100-p)

d = 5% absolute precision

On substituting, in the formula n = 3.84 x 11.3 x 88.7 / 25; n = 154

Adding 10% non-response rate (ie 10% of 154 = 15) n = 169 (minimum sample size) Therefore, Sample size n = 170 (1 group).

Sampling Procedure: By Convenience sampling

Ethical Approval: This study was approved by the Institutional Ethics Committee (IEC) – Govt. Stanley medical college. After obtaining permission from H.O.D of medicine and Diabetology dept., the study was conducted. Participants were informed about the purpose of the study. Written informed consent was obtained from participants. The participants were assured that the information details obtained will be only for research purposes and would therefore be anonymous and kept strictly confidential.

Data Collection Method

After obtaining the necessary permission, the study was conducted by the investigator. The general information of DM patient and DM disorder related factors were recorded using questionnaire and with use of their diabetic records. Then urine and blood samples were taking for necessary lab investigations. Then MMSE and MOCA scales were administered to assess cognitive impairment.

Data Collection Instruments

1. **Questionnaire**

- Pretested semi-structured questionnaire: (Annexure). It was orally administered to obtain general information of participants and disease related factors.
- Standard scales used: (Annexures). MMSE and MOCA scale for cognitive impairment

2. **Lab Investigations**

Urine albumin to assess proteinuria by using urine protein dipstick test

FBS and PPBS: to assess blood glucose control

Study Variables- Measurement and Operational Definitions

1. **Cognitive Impairment:** If participant has score less than 24 using MMSE scale or score less than 26 using MOCA scale, then patient was considered to have cognitive impairment.
2. **Age:** Completed age of participant as on date of the study in years
3. **Gender:** Male, female, or others
4. **No. of Hypoglycemic Episodes:** Participant with one or more symptoms like an irregular or fast heartbeat, fatigue, sweating, anxiety, hunger, irritabliltiy, confusion, blurred vision, seizures, loss of consciousness in the past one year were considered to have hypoglycemia
5. **Duration of Diabetes:** This was recorded in number of months and categorized as less than one year, 1-5 year and more than 5 year duration.
6. **Therapy:** This was recorded as per patients history of intake of Oral hypoglycemic drug and use of insulin. This variable is categorized as patient on OHA or patient on OHA+Insulin
7. **Uncontrolled Diabetes:** If participant has either fbs level > 130 mg/dl or PPBS level > 180 mg/dl then he/she was considered to have uncontrolled glucose level or uncontrolled diabetes
8. **Proteinuria:** If participant has albumin in urine of 1+ or more than 1+ then participant was considered to have proteinuria.

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Data Analysis

The data collected for cognitive impairment was scored as per concerned scales. Then all data were entered in MS Excel and analyzed using SPSS 22 version. Prevalence of categorical variables are given as proportions. MMSE, MOCA, FBS, PPBS values were given in both proportions and mean with S.D. Bivariate analysis was done by using Chi-square test/fisher exact test to find the significant predictors of cognitive impairment in DM patients. The p-value ($p<0.05$) considered significant.

RESULTS

A cross-sectional study was conducted among 170 Diabetes mellitus cases to assess the prevalence of cognitive impairment in tertiary care hospital in Chennai. The results of this study was given in following subheadings

1. Sociodemographic details of study participants
2. Cognitive impairment details
3. DM related factors
4. Association of sociodemographic and DM related factors with Cognitive impairment

Sociodemographic Details of Study Particpants

Table 1: Age distribution of study participants (N=170)

Age Group	n	%
31-35 years	7	4.1
36-40 years	23	13.5
41-45 years	53	31.2
46-50 years	87	51.2

Figure 1: Distribution of Age of Participants

The above table shows that majority of our study participants (82.4%) were above the age of 40 years. Only 30 out of 170 participants were below age of 40 years.

Table 2: Gender distribution of study participants (n=170)

GENDER	n	%
Female	67	39.4
Male	103	60.6

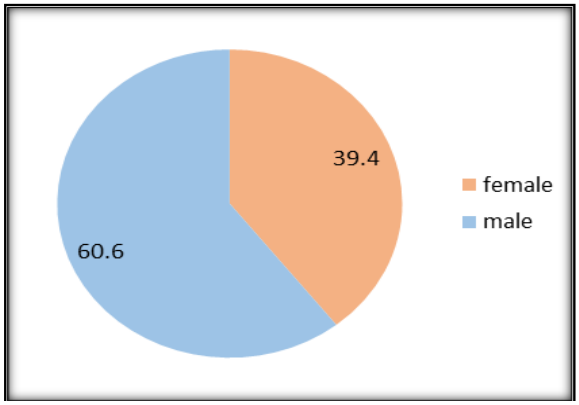

Figure 2: distribution of gender among study participants (n=170)

The above figure shown that majority of the participants were male with 60.6%.

Details of Cognitive Impairment

Table 3: distribution as per MMSE score

MMSE SCORE	N	%
<24	17	10
>24	153	90

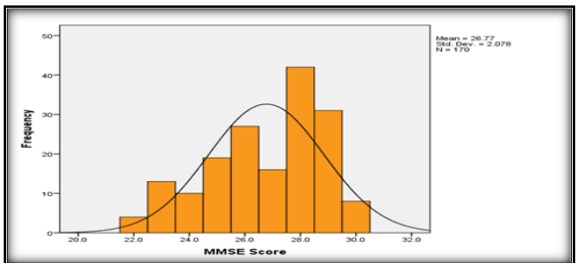

Figure 3: distribution of MMSE score

Above figure and table shows that 90% of participants have MMSE score above or equal to 24 and 10% below score 24. The score below 24 were considered to have cognitive impairment. The mean and s.d score of MMSE is 26.77+2.07.

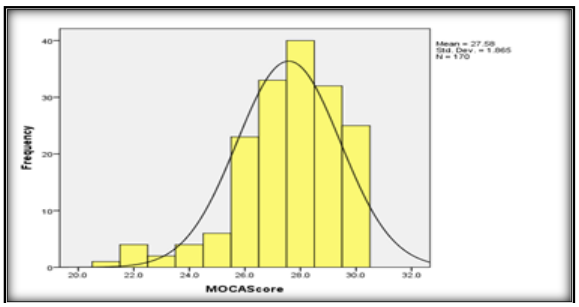

Figure 4: distribution of MOCA score

Table 4: distribution of study participants as per MOCA score (n-170)

MOCA SCORE	N	%
<26	17	10
>26	153	90

The MOCA score above 26 and above were considered to have normal cognition and score less than 26 were considered to have cognitive impairment.

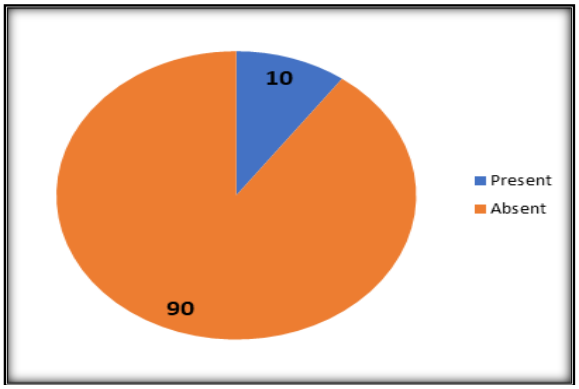

Figure 5: distribution of cognitive impairment (n=170)

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The prevalence of cognitive impairment in our study participants was 10% as per both MMSE and MOCA score. [Figure 5]

Details of DM Related Factors

Table 5: distribution of hypoglycemic episodes in our study(n=170)

No. of hypoglycemic episodes	n	%
0	141	82.9
1	23	13.5
2	5	2.9
3	1	.6

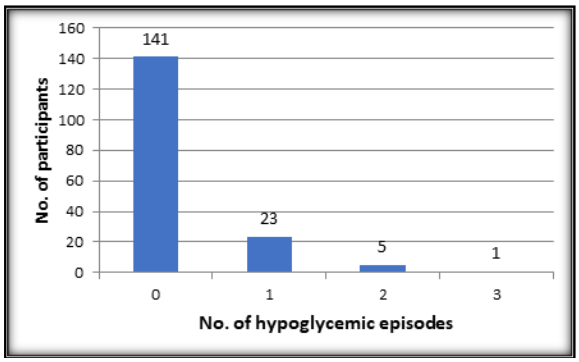

Figure 6: distribution of hypoglycemic episodes (n=170)

The [Table 5 and Figure 6] shows that majority of them around 141 participants had no episode of hypoglycemia in last one year, 23 had one episode and only one patient had three episode.

Table 6: distribution as per duration of DM (n=170)

Duration of DM	N	%
<1yr	13	7.6
1-5yr	141	82.9
>5yr	16	9.4

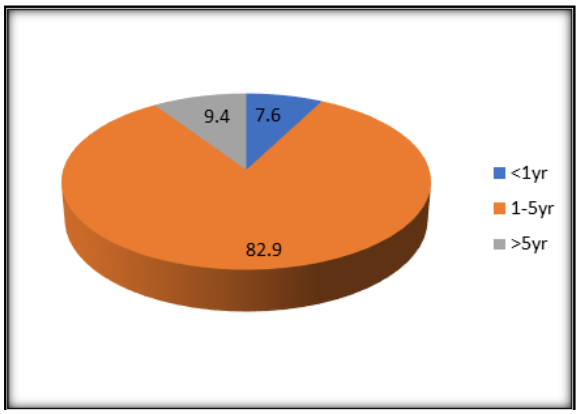

Figure 7: distribution as per duration of DM (N=170)

The above figure and table shows that 82.9% of the study participants had diabetes for duration 1-5 years. Only 7.6% had duration of less than one year

Table 7: distribution of uncontrolled glucose levels (n=170)

Blood glucose levels	N	%
Controlled	131	77.1
Uncontrolled	39	22.9

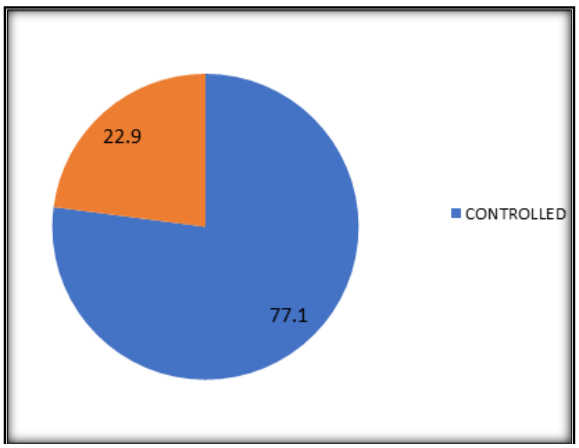

Figure 8: distribution as per uncontrolled glucose levels(n-170)

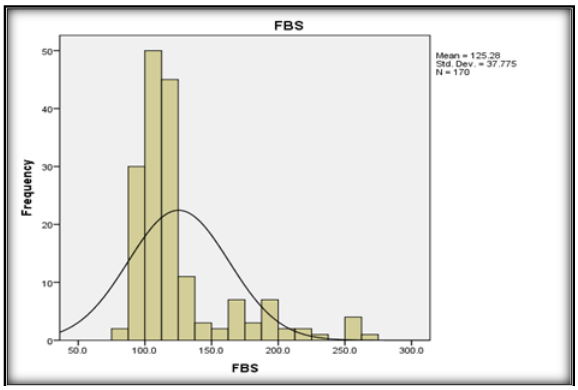

Figure 9a: mean and S.D of FBS values

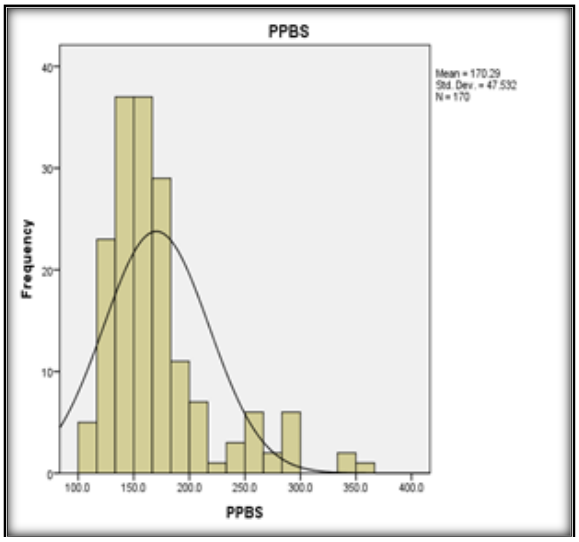

Figure 9b: mean and S.D of PPBS values

The [Figure 8] shows 22.9% of uncontrolled diabetes mellitus and [Figure 9] shows the mean fbs and ppbs levels of study participants to be 125.2 and 170.29. The cut off value for uncontrolled DM is FBS > 130 and PPBS >180mg/dl.

Table 8: distribution of participants as per treatment (n=170)

TREATMENT	N	%
OHA	147	86.5
OHA + INSULIN	23	13.5

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The above table shows that 86.5% were only on oral hypoglycemica and only 23 needed additional insulin therapy.

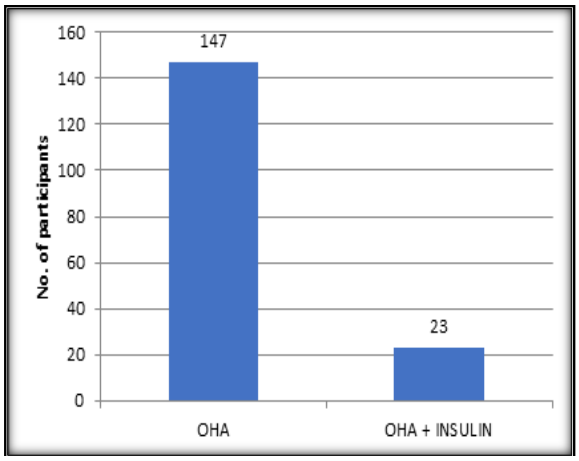

Figure 10: distribution as per treatment

Table 9: proteinuria distribution among participants (n=170)

Urine albumin (Proteinuria)	n	%
No	152	89.4
Yes	18	10.6

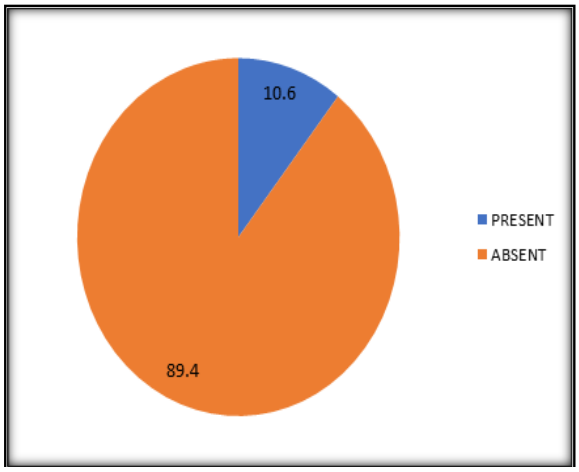

Figure 11: Distribution of Proteinuria

Table 10: association of age with cognitive impairment

Age group	Cognitive impairment			p value*
		Present	Absent	
31-35yr	n	0	7	0.530
	%	0.0%	100.0%	
36-40yr	n	1	22	
	%	4.3%	95.7%	
41-45yr	n	7	46	
	%	13.2%	86.8%	
45-50yr	n	9	78	
	%	10.3%	89.7%	

*Fisher exact test done as more than 20% of the cells has expected cell value less than 5.

The [Table 10 and Figure 12] shows that there was higher prevalence of cognitive impairment in ages above 41 years but the results were not statistically significant.

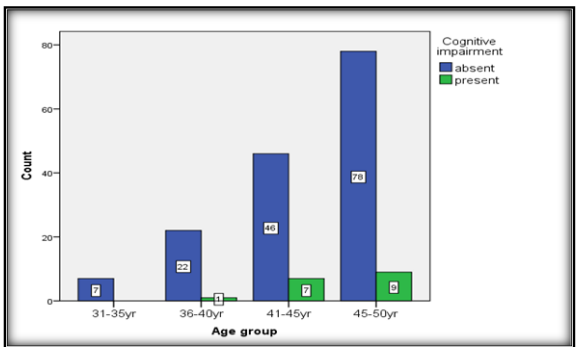

Figure 12: comparison of age with cognitive impairment.

Table 11: association of gender with cognitive impairment

GENDER	Cognitive impairment			p value
		Absent	Present	
Female	n	60	7	0.875
	%	89.6%	10.4%	
Male	n	93	10	
	%	90.3%	9.7%	

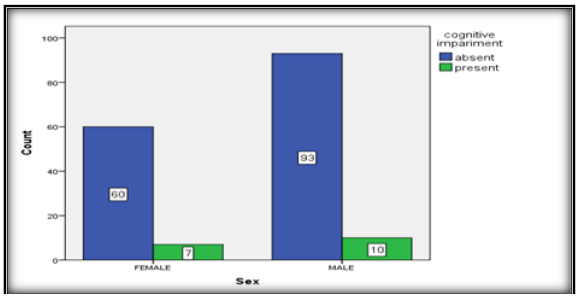

Figure 13: association of gender with cognitive impairment

The above figure and table shows there is no significant association of gender with cognitive impairment in our study as p less than 0.05.

Table 12: association of cognitive impairment with diabetic control

Diabetic control	Present (n,%)	Absent (n,%)	p value
Controlled	6, 4.6%	125, 95.4%	<0.001
Uncontrolled	11, 28.2%	11,71.8%	

[Table 12] shows patients with uncontrolled glucose level have significantly higher prevalence of cognitive impairment compared to controlled glucose level patients and p value is less than 0.001.

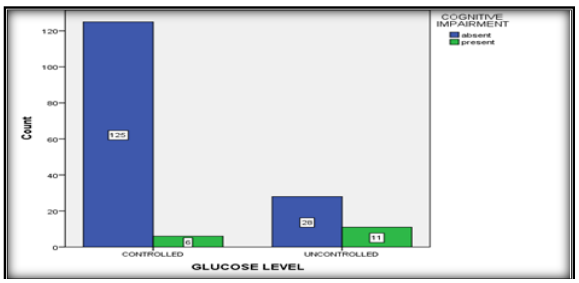

Figure 14: comparison of cognitive impairment with diabetic control

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Table 13: association of cognitive impairment with no of hypoglycemic control

No. Of hypoglycemic episodes		Cognitive Impairment		p value
		Present	Absent	
0	n	10	131	0.035
	%	7.1%	92.9%	
1	n	6	17	
	%	26.1%	73.9%	
2	n	1	4	
	%	20.0%	80.0%	
3	n	0	1	
	%	0.0%	100.0%	

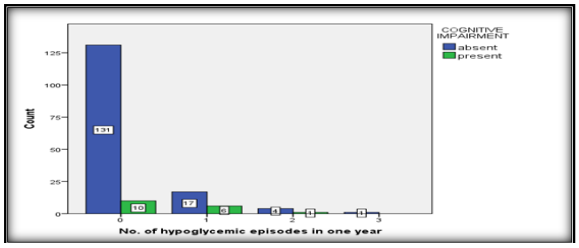

Figure 15: comparison of hypoglycemic episodes with cognitive impairment

The above table shows that there is significantly higher prevalence of cognitive impairment among patients with one or more hypoglycemic episodes compared to no hypoglycemic episodes.

Table 14: association of duration of dm with cognitive impairment

Duration of DM		Cognitive Impairment		
		Present	Absent	p value
<1yr	n	3	10	0.245
	%	23.1%	76.9%	
1-5yr	n	13	128	
	%	9.2%	90.8%	
>5yr	n	1	15	
	%	6.3%	93.8%	

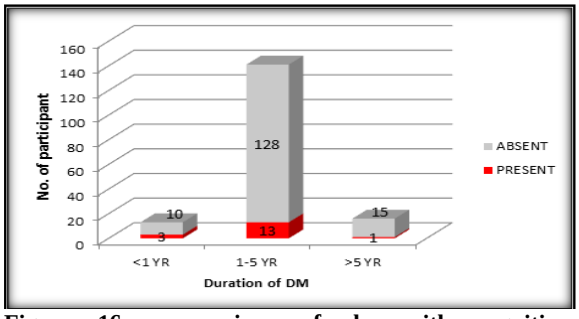

Figure 16: comparison of dm with cognitive impairment

The above table shows there is no significant association of duration of DM with cognitive impairment.

Table 15: association of proteinuria with cognitive impairment

Proteinuria		Cognitive impairment		P value
		Present	Absent	
Absent	Count	15	137	0.695
	%	9.9%	90.1%	
Present	Count	2	16	
	%	11.1%	88.9%	

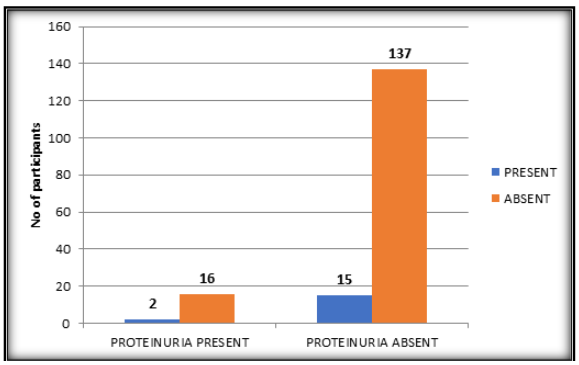

Figure 17: comparison of proteinuria with cognitive impairment

Table 16: comparison of cognitive impairment with

Treatment		Cognitive impairment		p value
		Present	Absent	
OHA	Count	12	135	0.054
	%	8.2%	91.8%	
OHA+INSULIN	Count	5	18	
	%	21.7%	78.3%	

The above figure and table shows there is no significant association of proteinuria with cognitive impairment.

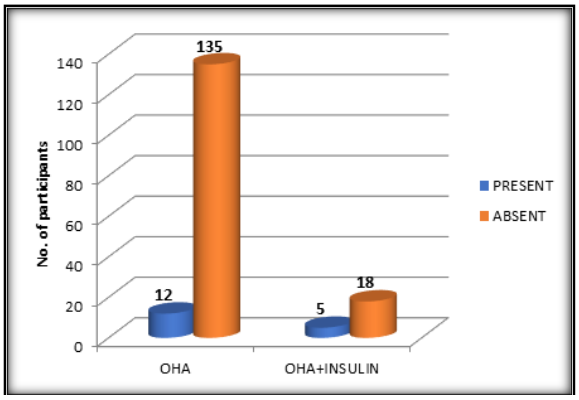

Figure 18: comparison of cognitive impairment with dm treatment

In our study, the participants with OHA with insulin treatment had higher prevalence of cognitive impairment compared to participants on OHA treatment alone and the results were not statistically significant.

DISCUSSION

A cross-sectional study was conducted in Tertiary care hospital, Chennai on assessing the prevalence of cognitive impairment in Type 2 Diabetes mellitus. The study was conducted among 170 DM patients.

Socio-demographic details of the study participants: In our study, the age of 31 years to 50 years were enrolled for assessment. Only 4.1% were belonging to age less than 35 years. Majority of the participants around 82.4% were above age 41years.

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The gender distribution shows 103 males and 67 females.

Cognitive Impairment

As per MMSE score, the mean score in our study participants was 26.7 with S.D 2.07. The score below 24 were considered to have cognitive impairment. Around 17 participants of around 10% had cognitive impairment. Score 18-23 were considered to have mild cognitive impairment. Those less than 17 were considered to have severe cognitive impairment. In our study none of the participants had severe cognitive impairment as per MMSE scale

As per MOCA score, the mean score in our study participants was 27.5 with S.D 1.86. The score below 26 were considered to have cognitive impairment. Around 17 participants of around 10% had cognitive impairment. The participants who were diagnosed to have cognitive impairment as per MOCA score were also diagnosed to have cognitive impairment as per MMSE score.

A study conducted among 194 diabetic subjects in rural field practice area in India, 50.5% of the participants had cognitive impairment. This difference in proportion from our study results might be attributed to the reason that the difference in age group as in this rural Indian study, the age group is from 40-65 years where as in our study age of 30-50 years were enrolled. And also difference in study setting where this is a field study and our's is an hospital study might have distorted the similarity in results.[10]

Another study by Roy et al, 82 patients with Type 2 DM were enroled in this study, the incidence of cognitive impairment was 19%. The results were similar to our study results.[11]

In our study, we have used both the scales-MMSE and MOCA to assess cognitive impairment. But the prevalence of cognitive impairment was assessed if the patients was diagnosed at least in one scale to have cognitive impairment.

The MMSE and the MoCA are both 30-point grading scale cognitive screening assessments. Both are quick, albeit the MMSE is a little quicker, taking about seven to eight minutes to complete. It takes about 10 to 12 minutes to complete the MoCA. Neither test is highly detailed, therefore it's likely that they'll only be utilised for preliminary screening. Both tests, as well as a variety of others in combination, are administered by several memory clinics and neurologists. Their various degrees of sensitivity make the most difference and will most likely be the deciding factor in which one is used.

"The MoCA is the best test for mild impairment," says Abhay Moghekar, MBBS, an assistant professor of neurology at Baltimore's Johns Hopkins University School of Medicine. "The MoCA does a great job of distinguishing between normal cognition and mild impairment or dementia, but it's too difficult to use for moderate to severe problems," explains Barbara Messinger-Rapport, MD, PhD, director of the Cleveland Clinic's Center for Geriatric Medicine. Overall, the MMSE is a better test for more severe disorders, although all tests have a ceiling and floor effect, according to Messinger-Rapport. "The MMSE ceiling is that a well-educated person can do well on the MMSE." In this context, since both scales are equally useful in assessing cognitive impairment both scales were used in our study.[12]

Diabetes Mellitus Disorder Related Factors

The study results shows that majority of them around 141 participants had no episode of hypoglycemia in last one year, 23 had one episode and only one patient had three episode. Similar to our study results, a retrospective study done by Miller et al., in among 1055 type 2 DM patients stated the prevalence of hypoglycemic episode is 24.5% where as our study shows 19.1% prevalence of hypoglycemic episode.[13]

Hypoglycemia is a serious side effect of diabetes treatment. While mild hypoglycemia creates unpleasant symptoms and interferes with patients' normal activities as it interferes with cognition and also severe hypoglycemia can lead to coma, seizures, and death. Recurrent episodes of mild hypoglycemia can also modify the counter regulatory response to lower blood glucose levels, leading to hypoglycemia unawareness, putting patients at risk for severe hypoglycemia. Recurrent hypoglycemia has also been linked to a reduction in diabetes patients' quality of life and cognition.[14]

In our study, 82.9% of the study participants had diabetes for duration 1-5 years. Only 7.6% had duration of less than one year.

In our study, 22.9% of uncontrolled diabetes mellitus and fig.9 shows the mean Fbs and Ppbs levels of study participants to be 125.2 and 170.29 mg/dl. The cut off value for uncontrolled DM is FBS > 130 and PPBS >180mg/dl.[15]

The cross-sectional study on prevalence of Uncontrolled DM in Pakistan, 2003 has shown prevalence results with 39%.[16] The under representation in our study results may be due to difference in study setting as the accessability and affordability of drugs and insulin is much better in our country compared to the previous study setting. And also the difference in sample size and methodology might have distorted the prevalence results similarities.

Another study by Sakboonyarat et al., on trends in uncontrolled diabetes by Hba1c levels have shown the prevalence of uncontrolled diabetes was 33-35.6% from 2011-18.[17] The difference in use of operational definition in diagnosing hypoglycemia between two studies.

In our study results shows that 86.5% were only on oral hypoglycemica and only 23 needed additional insulin therapy and only 10.6% had proteinuria

Association of cognitive impairment and other factors studied:

Age and Cognitive Impairment

In our study, there was higher prevalence of cognitive impairment in ages above 41 years but the

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results were not statistically significant. The majority of investigations on type 2 diabetes patients with decreased cognitive function have included older people (over 60 years old).18 It has been suggested that age-related cognitive impairment occurs most frequently after the age of 65, with a prevalence of 10-20%.[12]

Thus, even in the absence of type 2 diabetes, cognitive deterioration can be expected after 60 years of age as part of normal ageing.[11] This can be explained in a variety of ways. To begin with, growing senile is a risk factor for cognitive deterioration. The formation of senile plaques, which cause neuronal death through apoptosis, is a hallmark of ageing. This further causes cerebral cortical atrophy and, as a result, cognitive impairment. Second, various causes of cognitive dysfunction, such as stroke, dyslipidemia, hypertension, and heart disorders, are linked to ageing.[18]

According to Rosebud O. Roberts et al., diabetes beginning before the age of 65 years has correlation with mild cognitive impairment.[19] Roy et al. studied cognitive performance in type 2 diabetes patients aged 60 years or younger and reported that cognitive deterioration affects one-fifth of those in this age range and is linked to glycemic management and type 2 diabetes duration.[11]

Rajesh et al., investigated the cognitive condition of type 2 diabetes patients of various ages. They reported a substantial difference in mean MMSE scores between age groups, with patients over 60 years showing the most deterioration in cognition.[20] In their study, S.C. Tiwari et al. found that type 2 diabetes is a risk factor for cognitive impairment regardless of the cut-off age of 60 or 55 years.[21]

Gender and Cognitive Impairment

There were no significant association of gender with cognitive impairment. Similarly, a study by Priyam Mukherjee et al. found that cognitive impairment is linked to diabetes and that there is no significant link between patient sex and cognitive decline.[22]

In contrast to the aforementioned findings, Jie Ding et al. discovered a significant relationship between diabetic retinopathy and multiple cognitive measures solely in men in their investigation. They suggested that the lower prevalence of diabetes complications in women compared to males may influence the sex-specific effect of diabetic retinopathy on cognitive performance. When macrovascular illness was taken into account, there was no correlation between sex and cognitive function.[23]

In the study by Rajesh et al., found that diabetic women are more at risk than men to experience cognitive loss due to diabetes-related complications.[20]

The difference in study results may be due to difference in sample size and methodology between studies.

Uncontrolled Diabetes and Cognitive Impairment: The results in [Table 12] shows patients with uncontrolled glucose level have significantly higher prevalence of cognitive impairment compared to controlled glucose level patients and p value is less than 0.001.

Roy et al. discovered a link between HbA1c levels and cognitive impairment in type 2 diabetics aged 26 to 60 years. They found that 11.6 percent of those who had good glycemic control and 30.2 percent of those who had poor glycemic control had cognitive decline. Overall, there was a association between poor glycemic management and cognitive impairment.58 According to Oguz Tekin et al., high HbA1c levels which is an indicator of poor glycemic control is an additional risk factor for cognitive impairment.[23]

In their study, Tuligenga et al. discovered that poor glycemic control is connected to quicker cognitive deterioration.[24] Orchard et al., showed that cumulative glycemic exposure (the intensity and duration of hyperglycemia) is significant for microvascular problems and the risk of cognitive dysfunction.[25]

Rajeshkanna et al., investigated the link between decreased cognition and glycemic management in type 2 diabetes patients. They discovered a significant reduction in cognitive abilities in people with higher HbA1c levels.[26]

Duration of DM and Cognitive Impairment: The results in our study shows that there is no significant association of cognitive impairment with duration of DM in our study but there was significantly higher prevalence of cognitive impairment among patients with one or more hypoglycemic episodes compared to no hypoglycemic episodes.

According to a study by Divya Yogi-Morren et al. Subjects with a long history of DM performed badly on tests of working memory, fundamental attention, and executive function in MMSE scale.76 Rosebud O. Roberts et al. looked at the link between the duration of type 2 diabetes and cognitive damage, and found that the longer the period, the worse the cognitive outcome.[19]

Longer duration of type2 DM has significant correlation to macro vascular disease and brain infarction, white matter hyper intensities, which will impair cognitive function. Long term exposure to increased blood glucose might hasten the cognitive decline. Thus duration of diabetes might be vital in the pathogenesis of cognitive dysfunction in type2 DM.[9]

In our study, the non significant relation may be due to small sample size. So, a study with large sample size in future might bring out the appropriate proportion and association of duration of DM and cognition in DM patients.

Hypoglycemic Episodes and Cognitive Impairment: There was significantly higher prevalence of cognitive impairment among patients with one or more hypoglycemic episodes compared to no hypoglycemic episodes in our study.

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Hypoglycemia may raise the risk of future cognitive impairment through a variety of ways. Severe hypoglycemia can have long-term neurological consequences, such as neuronal cell death, which can hasten the onset of dementia. Hypoglycemia also boosts platelet aggregation and fibrinogen production, which could hasten vascular impairment in the brain. Hypoglycemic coma damages subiculum dentate, and granule cell sections of the hippocampus, which are crucial for learning and memory. Repeated episodes of hypoglycemia may have an impact on cognition by causing damage to these areas, especially in brains.[29]

Proteinuria & treatment modalities with cognitive impairment: In our study proteinuria and treatment modalities had no significant association with cognitive impairment.

Studies have shown albuminuria is associated with cognitive impairment. A TRANSCEND study by Barzilay et al., where a total of 28,384 people with vascular disease or diabetes were investigated using Mini-Mental State Examination (MMSE) and albumin excretion testing in their urine at baseline and at 5 years showed results that albuminuria is related with cognitive decline. The same study reported that participants with microalbuminuria and macroalbuminuria were having increased odds than those with normoalbuminuria to have a lower MMSE score. When compared to those with normoalbuminuria, those with baseline albuminuria had a higher risk of cognitive deterioration (a 3 point fall in MMSE score). When compared to those who remained normoalbuminuric, those who developed new albuminuria had a higher risk of cognitive decline throughout follow-up.[31]

The results of our study shows

- The prevalence of cognitive impairment in Type 2 DM patients is 10%
- The increased in number of hypoglycemic episodes and uncontrolled diabetes had significant risk of cognitive impairment in Diabetes patients.
- Age, gender, duration of DM, proteinuria, treatment modalities had no significant association with cognition impairment in our study

Limitations

- Single centre study which might limit the generalisability of study results
- Small sample size might have distorted the actual relation of some study factors
- This is a cross sectional study. Further follow up study is recommended to get a detailed picture of the cognitive function worsening over time in DM patients

CONCLUSION

Summary

A cross-sectional study was conducted among 170 Type 2 Diabetes patients attending medicine and diabetology department in Govt. Stanley Medical college, Chennai. By convenience sampling, 170 paritcipants between age of 30-50 were enrolled. The main objective of the study was –

Primary objective:

- To estimate the prevalence of cognitive impairment in patients with T2DM

Secondary objective:

- To determine presence of correlation between cognitive impairment and its severity with the duration of disease
- To determine presence of correlation between patients with cognitive impairment and frequency of hypoglycaemic episodes
- To determine the presence of correlation between proteinuria and cognitive impairment
- To determine the presence of correlation between cognitive impairment and grade of blood sugar control

The data was collected using MMSE and MOCA scale for cognitive impairment, blood glucose and urine albumin lab investigation and questionnaire for general information. The data collected were analysed using SPSS-22.

The results of our study is:

1. Majority of our study participants (82.4%) were above the age of 40 years. Only 30 out of 170 participants were below age of 40 years. majority of the participants were male with 60.6%.
2. 90% of participants have MMSE score above or equal to 24 and 10% below score 24. The score below 24 were considered to have cognitive impairment. The mean and s.d score of MMSE is 26.77+2.07.
3. The MOCA score above 26 and above were 90% and score less than 26 was 10%
4. The prevalence of cognitive impairment in our study participants was 10% as per both MMSE and MOCA score.
5. The majority of them around 141 participants had 0 episode of hypoglycemia in last one year, 23 had one episode and only one patient had three episode. 82.9% of had diabetes for duration 1-5 years. Only 7.6% had duration of less than one year
6. 22.9% of uncontrolled diabetes mellitus and the mean fbs and ppbs levels of study participants to be 125.2 and 170.29 mg/dl.
7. 86.5% were only on oral hypoglycemica and only 23 needed additional insulin therapy.
8. Age and gender have no significant relation with cognitive impairment
9. Patients with uncontrolled glucose level have significantly higher prevalence of cognitive impairment compared to controlled glucose level patients
10. There is significantly higher prevalence of cognitive impairment among patients with one or more hypoglycemic episodes compared to no hypoglycemic episodes.

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11. The treatment modalities, duration of disease and proteinuria have no significant association with cognitive impairment.

Conclusion

The prevalence of 10% of cognitive impairment in our study results suggest a need of routine cognitive function screening in individuals with Type 2 DM for early detection. hence, prompt psychosocial interventions can be adopted to prevent further cognitive function deterioration.

REFERENCES

1. Diabetes: Symptoms, Causes, Treatment, Prevention, and More [Internet]. [cited 2021 Dec 17]. Available from: https://www.healthline.com/health/diabetes
2. International Diabetes Federation. IDF Diabetes Atlas, 6th edn. Brussels, Belgium: International Diabetes Federation; 2013. http://www.idf.org/diabetesatlas
3. Kodl CT, Seaquist ER. Cognitive Dysfunction and Diabetes Mellitus. Endocrine Reviews. The Endocrine Society; 2008 Jun;29(4):494–511.
4. Taylor VH, Macqueen GM. Cognitive dysfunction associated with metabolic syndrome. Obesity Reviews. Wiley-Blackwell;2007 Sep;8(5):409-18.
5. Hsu C-C, Wahlqvist ML, Lee M-S, Tsai H-N. Incidence of dementia is increased in type 2 diabetes and reduced by the use of sulfonylureas and metformin. J Alzheimers Dis. 2011;24(3):485–93.
6. Diabetes mellitus in the young and the old: Effects on cognitive functioning across the life span - ScienceDirect [Internet]. [cited 2021 Dec 17]. Available from: https://www.sciencedirect.com/science/article/pii/S0969996119302839
7. Cukierman-Yaffe T, Gerstein HC, Williamson JD, Lazar RM, Lovato L, Miller ME, et al. Relationship Between Baseline Glycemic Control and Cognitive Function in Individuals With Type 2 Diabetes and Other Cardiovascular Risk Factors: The Action to Control Cardiovascular Risk in Diabetes-Memory in Diabetes (ACCORDMIND) trial. Diabetes Care. American Diabetes Association; 2009 Jan 26;32(2):221–6.
8. Lu F-P, Lin K-P, Kuo H-K. Diabetes and the Risk of Multi-System Aging Phenotypes: A Systematic Review and Meta-Analysis. PLOS ONE [Internet]. 2009 Jan 7 [cited 2021 Dec 17];4(1):e4144. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0004144
9. Murray AM, Hsu F-C, Williamson JD, Bryan RN, Gerstein HC, Sullivan MD, et al. ACCORDION MIND: results of the observational extension of the ACCORD MIND randomised trial. Diabetologia [Internet]. 2017 Jan [cited 2021 Dec 17];60(1):69–80. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5633725/
10. Yerrapragada DB, Rao CR, Karunakaran K, Lee HSE. Cognitive Dysfunction Among Adults With Type 2 Diabetes Mellitus in Karnataka, India. Ochsner J [Internet]. 2019 [cited 2021 Dec 17];19(3):227–34. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6735609/
11. Roy S, Kim N, Desai A, Komaragiri M, Baxi N, Jassil N, et al. Cognitive Function and Control of Type 2 Diabetes Mellitus in Young Adults. N Am J Med Sci [Internet]. 2015 May [cited 2021 Dec 17];7(5):220–6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4462818/
12. MMSE vs. MoCA: What You Should Know [Internet]. [cited 2021 Dec 17]. Available from: https://www.todaysgeriatricmedicine.com/news/ex_012511_01.shtml
13. Miller CD, Phillips LS, Ziemer DC, Gallina DL, Cook CB, El-Kebbi IM. Hypoglycemia in Patients With Type 2 Diabetes Mellitus. Archives of Internal Medicine [Internet]. 2001 Jul 9 [cited 2021 Dec 17];161(13):1653–9. Available from: https://doi.org/10.1001/archinte.161.13.1653
14. Influence of Intensive Diabetes Treatment on Quality-of-Life Outcomes in the Diabetes Control and Complications Trial | Diabetes Care [Internet]. [cited 2021 Dec 17]. Available from: https://care.diabetesjournals.org/content/19/3/195
15. Symptoms of Uncontrolled Diabetes [Internet]. Verywell Health. [cited 2021 Dec 17]. Available from: https://www.verywellhealth.com/uncontrolled-diabetes-symptoms-5120437
16. Siddiqui FJ, Avan BI, Mahmud S, Nanan DJ, Jabbar A, Assam PN. Uncontrolled diabetes mellitus: Prevalence and risk factors among people with type 2 diabetes mellitus in an Urban District of Karachi, Pakistan. Diabetes Research and Clinical Practice [Internet]. 2015 Jan 1 [cited 2021 Dec 17];107(1):148–56. Available from: https://www.sciencedirect.com/science/article/pii/S0168222714004252
17. Sakboonyarat B, Pima W, Chokbumrungsuk C, Pimpak T, Khunsri S, Ukritchon S, et al. National trends in the prevalence of glycemic control among patients with type 2 diabetes receiving continuous care in Thailand from 2011 to 2018. Sci Rep [Internet]. 2021 Jul 12 [cited 2021 Dec 17];11(1):14260. Available from: https://www.nature.com/articles/s41598-021-93733-4
18. Dey J, Misra A, Desai NG, Mahapatra AK, Padma MV. Cognitive Function in Younger Type II Diabetes. Diabetes Care. American Diabetes Association; 1997 Jan 1;20(1):32–5.
19. O Eze C. The Prevalence of Cognitive Impairment amongst Type 2 Diabetes Mellitus Patients at Abakaliki South-East Nigeria. Journal of Metabolic Syndrome. OMICS Publishing Group; 2015;04(01)
20. Roberts RO, Geda YE, Knopman DS, Christianson TJH, Pankratz VS, Boeve BF, et al. Association of Duration and Severity of Diabetes Mellitus With Mild Cognitive Impairment. Archives of Neurology.American Medical Association (AMA) ; 2008 Aug 1;65(8)
21. V Rajesh, T Kannadasan and Vijayakumar P.R. Anand. Potential Risk factors for cognitive decline in diabetic cohort. International Journal of Pharma and bio sciences;jul-sept 2011;2(3).
22. Tripathi R, Farooqi S, Kumar R, Srivastava G, Kumar A, Tiwari S. Diabetes mellitus: A risk factor for cognitive impairment amongst urban older adults. Industrial Psychiatry Journal. Medknow; 2012;21(1):44.
23. Mukherjee Priyam, Mazumdar Srijan, Goswami Soumik, Bhowmik Jayeeta, Chakroborty Subhro, Mukhopadhyay Sumanto, Jana Subhendu, Chakraborty Amal, Pal Sandip, K.Das Shyamal, Mukhopadhyay Jotideb. Cognitive Dysfunction In Diabetic Patients With Special Reference To Age Of Onset, Duration And Control Of Diabetes. Activitas Nervosa Superior; 2012; 54(1-2).
24. Ding J, Strachan MWJ, Reynolds RM, Frier BM, Deary IJ, Gerald FFR, et al. Diabetic Retinopathy and Cognitive Decline in Older People With Type 2 Diabetes: The Edinburgh Type 2 Diabetes Study. Diabetes. American Diabetes Association; 2010 Aug 26;59(11):2883–9
25. Tekin Oguz, Cukur Serdar, Yigitoglu MR. cognitive impairment among type 2 diabetic subjects and its relationship with long term complications. Turk J Med Sci. 2009;39(5):661–9.
26. Tuligenga RH, Dugravot A, Tabák AG, Elbaz A, Brunner EJ, Kivimäki M, et al. Midlife type 2 diabetes and poor glycaemic control as risk factors for cognitive decline in early old age: a posthoc analysis of the Whitehall II cohort study. The Lancet Diabetes & Endocrinology. Elsevier BV; 2014 Mar;2(3):228–35.
27. Orchard TJ. Cumulative Glycemic Exposure and Microvascular Complications in Insulin-Dependent Diabetes Mellitus. Archives of Internal Medicine. American Medical Association (AMA); 1997 Sep 8;157(16):1851.
28. Rajeshkanna N, Valli S, Thuvaragah P. Relation between diabetes mellitus type 2 and cognitive impairment: A predictor of alzheimer's disease. International Journal of

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Medical Research & Health Sciences. Diva Enterprises Private; 2014;3(4):903.
29. Yogi-Morren D, Galioto R, Strandjord SE, Kennedy L, Manroa P, Kirwan JP, et al. Duration of Type 2 Diabetes and Very Low Density Lipoprotein Levels Are Associated with Cognitive Dysfunction in Metabolic Syndrome. Cardiovascular Psychiatry and Neurology. Hindawi Publishing; 2014;2014:1–6.
30. Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP, Selby JV. Hypoglycemic Episodes and Risk of Dementia in Older Patients with Type 2 Diabetes Mellitus. JAMA [Internet]. 2009 Apr 15 [cited 2021 Dec 17];301(15):1565–72. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2782622/
31. Barzilay JI, Gao P, O'Donnell M, Mann JF, Anderson C, Fagard R, Probstfield J, Dagenais GR, Teo K, Yusuf S; ONTARGET and TRANSCEND Investigators. Albuminuria and decline in cognitive function: The ONTARGET/TRANSCEND studies. Arch Intern Med. 2011 Jan 24;171(2):142-50. doi: 10.1001/archinternmed.2010.502. PMID: 21263104.

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